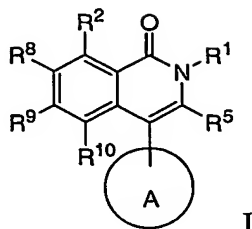


WHAT IS CLAIMED IS:

1. A compound of the structure:



- 5 or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

- a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO₂,

3) CN,

4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,

5) C≡C R⁴⁶,

6) (CRⁱR^j)_rOR⁴⁶,

7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),

8) (CRⁱR^j)_rC(O)R⁴⁶,

9) (CRⁱR^j)_rC(O)OR⁴⁶,

10) (CRⁱR^j)_rR⁴⁶,

11) (CRⁱR^j)_rS(O)₀₋₂R⁶¹,

12) (CRⁱR^j)_rS(O)₀₋₂N(R⁴⁶R⁴⁷),

13) OS(O)₀₋₂R⁶¹,

14) N(R⁴⁶)C(O)R⁴⁷,

15) N(R⁴⁶)S(O)₀₋₂R⁶¹,

16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,

17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,

18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),

19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,

20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),

21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or

22) oxo, or

b) a heteroaryl ring selected from the group consisting of

a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O and S, and

a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO₂,

3) CN,

4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,

5) C≡CR⁴⁶,

6) (CRⁱR^j)_rOR⁴⁶,

7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),

8) (CRⁱR^j)_r C(O)R⁴⁶,

9) (CRⁱR^j)_r C(O)OR⁴⁶,

10) (CRⁱR^j)_rR⁴⁶,

11) (CRⁱR^j)_r S(O)₀₋₂R⁶¹,

12) (CRⁱR^j)_r S(O)₀₋₂N(R⁴⁶R⁴⁷),

13) OS(O)₀₋₂R⁶¹,

14) N(R⁴⁶)C(O)R⁴⁷,

15) N(R⁴⁶)S(O)₀₋₂R⁶¹,

16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,

17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,

18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),

19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,

20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),

21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or

22) oxo;

R¹ is selected from the group consisting of

1) hydrogen,

2) (CR^aR^b)_nR⁴⁰

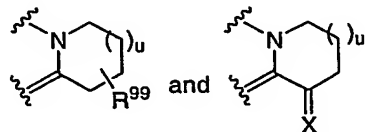
- 3) $(\text{CR}^a\text{R}^b)_n\text{OR}^{40}$,
- 4) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40}\text{R}^{41})$,
- 5) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40})\text{C}(\text{O})\text{OR}^{41}$,
- 6) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40})(\text{CR}^c\text{R}^d)_2\text{N}(\text{R}^{41})\text{C}(\text{O})\text{R}^{49}$,
- 7) C_{3-8} cycloalkyl,
- 8) $(\text{CR}^a\text{R}^b)_n\text{C}(\text{O})\text{OR}^{40}$,
- 9) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40})(\text{CR}^c\text{R}^d)_{1-3}\text{R}^{41}$,
- 10) $(\text{CR}^a\text{R}^b)_n\text{S}(\text{O})_{0-2}\text{R}^6$,
- 11) $(\text{CR}^a\text{R}^b)_n\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{40}\text{R}^{41})$,
- 12) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40})\text{R}^6\text{OR}^{41}$,
- 13) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40})(\text{CR}^c\text{R}^d)_{0-6}\text{C}(\text{O})\text{N}(\text{R}^{41}\text{R}^{42})$;

R^5 is selected from the group consisting of

- 1) hydrogen,
- 2) halogen,
- 3) $\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{53}\text{R}^{50})$,
- 4) $\text{S}(\text{O})_{0-2}\text{R}^{62}$,
- 5) CH_3 ,
- 6) $\text{C}_3\text{-C}_6$ alkyl,
- 7) $\text{C}_3\text{-C}_{10}$ cycloalkyl,
- 8) R^{82} ,

said alkyl, and cycloalkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ;

or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



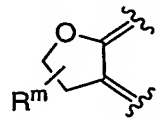
where u is 0 or 1, R^{99} is hydrogen or $-\text{OH}$, and X is O or =NOH ;

R^2 , R^8 , R^9 and R^{10} are independently selected from:

- 1) hydrogen,

- 2) halogen,
 3) NO₂,
 4) CN,
 5) CR⁴³=C(R⁴⁴R⁴⁵),
 6) C≡CR⁴³,
 7) (CR^eR^f)_pOR⁴³,
 8) (CR^eR^f)_pN(R⁴³R⁴⁴),
 9) (CR^eR^f)_pC(O)R⁴³,
 10) (CR^eR^f)_pC(O)OR⁴³,
 11) (CR^eR^f)_pR⁴³,
 12) (CR^eR^f)_pS(O)₀₋₂R⁶⁰,
 13) (CR^eR^f)_pS(O)₀₋₂N(R⁴³R⁴⁴),
 14) OS(O)₀₋₂R⁶⁰,
 15) N(R⁴³)C(O)R⁴⁴,
 16) N(R⁴³)S(O)₀₋₂R⁶⁰,
 17) (CR^eR^f)_pN(R⁴³)R⁶⁰,
 18) (CR^eR^f)_pN(R⁴³)R⁶⁰OR⁴⁴,
 19) (CR^eR^f)_pN(R⁴³)(CR^gR^h)_qC(O)N(R⁴⁴R⁴⁵),
 20) N(R⁴³)(CR^eR^f)_pR⁶⁰,
 21) N(R⁴³)(CR^eR^f)_pN(R⁴⁴R⁴⁵), and
 22) (CR^eR^f)_pC(O)N(R⁴³R⁴⁴),

or R² and R⁸ are independently as defined above, and R⁹ and R¹⁰, together with the atoms to which they are attached, form the ring



, where R^m is C₁₋₆alkyl;

- 25 Ra, R^b, R^c, R^d, R^e, R^f, R^g, R^h, Rⁱ, R^j, R^k, and R^l are independently selected from the group consisting of:

- 1) hydrogen,
 2) C₁-C₆ alkyl,
 3) halogen,
 4) aryl,
 5) R⁸⁰,
 6) C₃-C₁₀ cycloalkyl, and
 7) OR⁴,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R⁷, disubstituted with R⁷ and R¹⁵, trisubstituted with R⁷, R¹⁵ and R¹⁶, or tetrasubstituted with R⁷, R¹⁵, R¹⁶ and R¹⁷;

5

R⁴, R⁴⁰, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹, R⁵², and R⁵³ and are independently selected from the group consisting of

10

- 1) hydrogen,
- 2) C₁-C₆ alkyl,
- 3) C₃-C₁₀ cycloalkyl,
- 4) aryl,
- 5) R⁸¹,
- 6) CF₃,
- 7) C₂-C₆ alkenyl, and
- 8) C₂-C₆ alkynyl,

15

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R¹⁸, di-substituted with R¹⁸ and R¹⁹, tri-substituted with R¹⁸, R¹⁹ and R²⁰, or tetra-substituted with R¹⁸, R¹⁹, R²⁰ and R²¹;

20 R⁶, R⁶⁰, R⁶¹, R⁶² and R⁶³ are independently selected from the group consisting of

- 1) C₁-C₆ alkyl,
- 2) aryl,
- 3) R⁸³, and
- 4) C₃-C₁₀ cycloalkyl;

25

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R²⁶, di-substituted with R²⁶ and R²⁷, tri-substituted with R²⁶, R²⁷ and R²⁸, or tetra-substituted with R²⁶, R²⁷, R²⁸ and R²⁹;

R⁷, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, and R²⁹ are

30 independently selected from the group consisting of

- 1) C₁-C₆ alkyl,
- 2) halogen,
- 3) OR⁵¹,
- 4) CF₃,
- 5) aryl,

35

- 6) C₃-C₁₀ cycloalkyl,
- 7) R⁸⁴,
- 8) S(O)₀₋₂N(R⁵¹R⁵²),
- 9) C(O)OR⁵¹,
- 10) C(O)R⁵¹,
- 11) CN,
- 12) C(O)N(R⁵¹R⁵²),
- 13) N(R⁵¹)C(O)R⁵²,
- 14) S(O)₀₋₂R⁶³,
- 15) NO₂, and
- 16) N(R⁵¹R⁵²);

R⁸⁰, R⁸¹, R⁸², R⁸³ and R⁸⁴ are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6; provided that

when R⁹ is OCH₃, R¹ is CH₃ and R⁵ is C(CH₃)₃, then A is substituted,

when R⁹ is hydrogen, R¹ is CH₃, and R⁵ is hydrogen, then A is substituted,

when R⁹ is hydrogen, R¹ is CH₃, and R⁵ is C(CH₃)₃, then A is substituted, provided the substituent is not CH₃, and

when R⁹ is OCH₃, R¹ is CH₃, R⁵ is CH₃, then A is substituted.

2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein

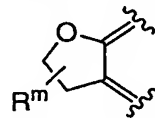
A is an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, or a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole;

R², R⁸, R⁹ and R¹⁰ are independently selected from the group consisting of:

- 1) hydrogen,
- 2) halogen,
- 3) OR⁴³,
- 4) (C(R^eR^f)_p)R⁴³,
- 5) CN, and

6) $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{N}(\text{R}^{43}\text{R}^{44})$,

or R^2 and R^8 are independently as defined above, and R^9 and R^{10} , together with the atoms to which they are attached, form the ring



, where R^m is C_{1-6} alkyl;

5 R^1 is selected from the group consisting of

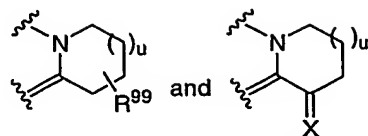
- 1) hydrogen,
- 2) $(\text{CR}^a\text{R}^b)_{1-2}\text{R}^{40}$
- 3) $(\text{CR}^a\text{R}^b)_{1-2}\text{OR}^{40}$,
- 4) $(\text{CR}^a\text{R}^b)_{1-2}\text{N}(\text{R}^{40}\text{R}^{41})$,
- 5) $(\text{CR}^a\text{R}^b)_{1-2}\text{N}(\text{R}^{40})\text{C}(\text{O})\text{OR}^{41}$,
- 6) $(\text{CR}^a\text{R}^b)_{1-2}\text{N}(\text{R}^{40})(\text{CR}^c\text{R}^d)_2\text{N}(\text{R}^{41})\text{C}(\text{O})\text{R}^{49}$,
- 7) $(\text{CR}^a\text{R}^b)_{1-2}\text{C}(\text{O})\text{OR}^{40}$,
- 8) $(\text{CR}^a\text{R}^b)_{1-2}\text{N}(\text{R}^{40})(\text{CR}^c\text{R}^d)_{1-3}\text{R}^{41}$, and
- 9) cyclopropyl; and

15 R^5 is selected from the group consisting of

- 1) hydrogen,
- 2) halogen,
- 3) $\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{53}\text{R}^{50})$,
- 4) $\text{S}(\text{O})_{0-2}\text{R}^{62}$,
- 5) CH_3 ,
- 6) $\text{C}_3\text{-C}_6$ alkyl,
- 7) $\text{C}_3\text{-C}_{10}$ cycloalkyl,
- 8) R^{82} ,

25 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ,

30 or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



where u is 0 or 1, R^{99} is hydrogen or $-OH$, and X is O or $\xi=NOH$.

3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein R^2 , R^8 , R^9 and R^{10} are independently selected from the group consisting of:

- 1) hydrogen,
- 2) halogen,
- 3) OR^{43} , and
- 4) $(CR^eR^f)_pC(O)N(R^{43}R^{44})$.

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of

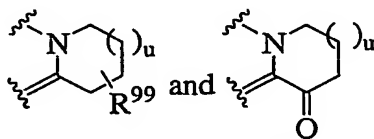
- 1) hydrogen,
- 2) $(CR^aR^b)_{1-2}R^{40}$
- 3) $(CR^aR^b)_{1-2}OR^{40}$, or
- 4) $(CR^aR^b)_{1-2}N(R^{40}R^{41})$;

R^5 is selected from the group consisting of

- 1) hydrogen,
- 2) C_3 - C_6 alkyl, and
- 3) CH_3 ,

said alkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ;

or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



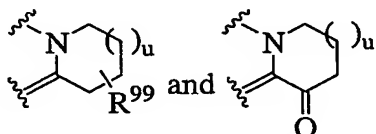
where u is 1, and R^{99} is hydrogen or $-OH$.

5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein A is unsubstituted phenyl, or phenyl substituted with halogen.

6. A compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from the group consisting of -CH₃, -CH₂CH₃, -(CH₂)₂OCH₃, -(CH₂)₂NH₂, and -(CH₂)₃NH₂, -CH₂C(O)OC(CH₃)₃; and

R⁵ is selected from the group consisting of hydrogen, -C(CH₃)₃, -CH₃,

or R¹ and R⁵ together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



where u is 1, and R⁹⁹ is hydrogen or -OH.

7. A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

3-tert-butyl-4-(3-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,

3-tert-butyl-4-(4-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,

6-methoxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

4-(3-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,

4-(4-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,

(1E)-11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione 1-oxime,

3-tert-butyl-6-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

2,3-dimethyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-ethyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

5 3-tert-butyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

2-ethyl-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

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6-methoxy-2-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1(2H)-one,

2-(2-aminoethyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

15 2-(3-aminopropyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carbonitrile,

3-tert-butyl-8-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

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3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carboxamide,

3-tert-butyl-2-methyl-4-phenyl-6-(4-phenylbutoxy)isoquinolin-1(2H)-one,

25 3-tert-butyl-2-methyl-4-phenyl-6-[(5-phenylpentyl)oxy]isoquinolin-1(2H)-one,

11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione,

(+/-)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

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(1S)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

(1*R*)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-*b*]isoquinolin-6-one,
and

11-(3-fluorophenyl)-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-*b*]isoquinolin-6-one.

5

8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by K_v1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting K_v1.5.

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9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

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11. A method of Claim 10, wherein the cardiac arrhythmia is atrial fibrillation.

12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by K_v1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting K_v1.5.

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13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

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15. A method of Claim 14, wherein the cardiac arrhythmia is atrial fibrillation.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

17. A method of Claim 16, wherein the thromboembolic event is a stroke.

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18. A method of Claim 12, wherein the condition is congestive heart failure.

19. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

5 21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta
10 inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

15 22. A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.